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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,649	10/07/2003	Robert A. Holton	FSUM 10442.19	5089

321 7590 07/29/2005

SENNIGER POWERS LEAVITT AND ROEDEL
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EXAMINER	
DELACROIX MUIRHEI, CYBILLE	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/680,649	HOLTON, ROBERT A.	
	Examiner	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The following is responsive to appellant 's brief received May 9, 2005.

Prosecution on the merits is reopened in view of the following new ground(s) of rejection.

Claims 1-20 are currently pending.

Applicant's arguments in the brief submitted May 9, 2005 traversing the previous rejection of claims 1-20 under 35 USC 103(a) maintained in the office action mailed Nov. 9, 2004 have been considered but are not found to be persuasive.

Said rejection is maintained essentially for the reasons given previously in the office actions mailed Nov. 9, 2004 and March 23, 2004 with the following additional comment:

Applicant submits that claim 1 is directed to a method of treating a patient afflicted with a cancer selected from the group consisting of breast, head, neck, esophageal, lung, and colon cancer by orally administering a pharmaceutical composition consisting essentially of a taxane, a solvent capable of dissolving the taxane, polyoxyethylatated castor oil, a diluent, and optionally a flavoring, wherein the taxane has a solubility in ethanol at room temperature of at least 200 mg/ml. Therefore, the method of claim 1 requires use of a taxane having a solubility in ethanol at room temperature of at least 200 mg/ml.

In contrast, Broder et al. and McChesney-Harris merely disclose formulations containing taxol (also known as paclitaxel). Taxol, however, does not have a solubility of ethanol of at least 200 mg/ml; rather, the solubility of taxol in ethanol is less than 40

mg/ml. Furthermore, Broder et al., McChesney-Harris, and Goodman and Gillman do not suggest that any advantages could be derived by selecting a taxane having a solubility in ethanol which is substantially greater than the solubility of taxol in ethanol. Additionally neither of the references discloses the benefits of solubility in ethanol or the relationship between improved taxane efficacy and its solubility in ethanol.

The cited references do not disclose or suggest that increased ethanol solubility of a taxane may be directly related to improved efficacy in treating cancer. Both Broder and McChesney-Harris disclose compositions to improve absorption and/or water solubility of a taxane. The references, at most, disclose that taxane insolubility in water is an obstacle to absorption or bioavailability, which is not equivalent to disclosing that improved ethanol solubility of a taxane is directly related to its efficacy in treating cancer. The modification of paclitaxel disclosed by McChesney-Harris was an attempt to increase its water solubility, not its ethanol solubility. Thus, the prior art attempts to modify the structure of paclitaxel were not related to applicant's understanding that improved ethanol solubility of taxane compounds are directly related to improved efficacy in treating cancer, but rather related to overcoming the obstacle of paclitaxel's precipitation in an aqueous solution. Finally, applicant asserts, the examiner used impermissible hindsight reconstruction to arrive at the claimed method.

Said arguments have been considered but are not found to be persuasive.

Broder and McChesney-Harris' disclosure of oral formulations containing taxol or paclitaxel falls outside the scope of the claimed method since the solubility of taxol in ethanol is less than 40 mg/ml. However, both Broder and McChesney-Harris disclose

oral formulations containing taxanes other than paclitaxel. In other words, the Broder and McChesney-Harris patents are not directed solely to the use of oral formulations containing paclitaxel. Broder et al. teach oral administration of the "taxane class of antineoplastic agents, in particular paclitaxel and its derivatives, analogs and prodrugs, and the semisynthetic paclitaxel analog docetaxel" (please see col. 6, lines 23-28). Please see also col. 7, lines 20-26, where Broder et al. disclose that the class of orally administered therapeutic agents are paclitaxel, other taxanes, docetaxel and derivatives and prodrugs of all of the foregoing, particularly their 2'-MPM salts and other 2'-methylpyridinium salts.

McChesney-Harris discloses novel methods and compositions for delivery of paclitaxel and other derivatives or their water insoluble derivatives (please see [0009]. Thus, the Examiner respectfully submits that, absent evidence to the contrary, the disclosed taxanes and water insoluble derivatives (other than paclitaxel) would obviously exhibit suitable solubility in ethanol to give the desired bioavailability. Applicant has not distinguished the taxane class of drugs disclosed in the prior art from the taxanes claimed in the instant application. Paclitaxel may fall outside the scope of the claims; however, applicant's arguments directed only to paclitaxel do not remove the entire class of taxanes taught by the prior art from the scope of the claimed invention.

Moreover, the prior art, which is analogous, recognizes the problem of limited solubility of taxanes. The references are in the same field of endeavor and the prior art is solving the same problem, i.e. limited solubility of taxanes. Please see In re Wood, 202 USPQ 171, 174 (CCPA 1979). The Examiner respectfully maintains that it would

have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the oral compositions used in the methods of Broder et al. and McChesney-Harris such that the taxane has sufficient solubility necessary to render the oral composition therapeutically effective. Absent evidence of unexpected results, such a modification would have been motivated by the reasonable expectation of producing an oral composition which when orally administered is readily bioavailable.

Additionally, applicant is arguing a difference in degree (solubility) not kind. The Examiner respectfully submits that these arguments do not clearly distinguish the claimed taxanes from those disclosed in the prior art. Applicant's arguments do not clarify whether the claimed solubility is a result of some structural feature of the claimed taxanes or whether the solubility is a result of the combination of excipients present in the claimed pharmaceutical composition.

Concerning applicant's argument that the prior art attempts to modify the structure of paclitaxel were not related to applicant's understanding that improved ethanol solubility of taxane compounds are directly related to improved efficacy in treating cancer; according to the MPEP 2144, "[t]he reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. In re Linter, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972); In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied, 500 U.S. 904 (1991)." In this case, the Examiner respectfully maintains that it would have been obvious to one of ordinary skill

in the art at the time the invention was made to further modify the oral compositions used in the methods of Broder et al. and McChesney-Harris such that the taxane has sufficient solubility necessary to render the oral composition therapeutically effective.

Finally, In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Claim Rejection(s)—35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The newly added claim 19, which recites treatment of esophageal cancer introduces new matter into the claims. There is neither explicit or implicit support the treatment of esophagus cancer using the claimed method.

Conclusion

Claims 1-20 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Cybille Delacroix-Muirheid** whose telephone number is **571-272-0572**. The examiner can normally be reached on Mon-Thurs. from 8:30 to 6:00 as well as every other Friday from 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Christopher Low**, can be reached on **571-272-0951**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CDM
July 25, 2005

REBECCA COOK
PRIMARY EXAMINER
GROUP 1200/1614